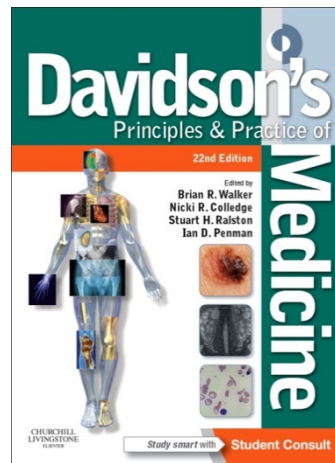
Davidson's Principles and Practice of Medicine

22 key points about the 22nd Edition

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1. Every chapter has been revised in detail by experts in the field to bring it up to date, and subjected to rigorous editorial review. The result is a book which is not increased in length, but contains all of the important contemporary updates in medical practice, presented with the clarity and simplicity that is Davidson's trademark.

2. A simplified classification provides a clearer presentation of the 1350 boxes used throughout the book. Popular **In Old Age**, **In Pregnancy**, **Emergency** and **Practice Point** boxes are retained while the **Evidence-Based Medicine** boxes which ensure that readers are aware of innovations in practice have been updated with descriptions of new guidelines.

19.26 Indications for assisted ventilation in acute severe asthma

- Coma
- Respiratory arrest
- Deterioration of arterial blood gas tensions despite optimal therapy
  - $PaO_2 < 8$ kPa (60 mmHg) and falling
  - $PaCO_2 > 6$ kPa (45 mmHg) and rising
  - pH low and falling (H^+ high and rising)
- Exhaustion, confusion, drowsiness

19.64 Factors predisposing to fungal disease

Systemic factors

- Diabetes mellitus
- Chronic alcoholism
- HIV
- Radiotherapy
- Corticosteroids and other immunosuppressant medication

Local factors

- Tissue damage by suppuration or necrosis
- Alteration of normal bacterial flora by antibiotic therapy

7.2 How to assess a Fried Frailty score

- Handgrip strength in bottom 20% of healthy elderly distribution*
- Walking speed in bottom 20% of healthy elderly distribution*
- Self-reported exhaustion
- Physically inactive
- At least 6 kg weight loss within 1 year

Patient is defined as frail if 3 or more factors are present.

*Varies between populations. Grip cutoff is 30 kg for men, 18 kg for women in US adults; 5 m walk time cutoff is 7 seconds in US adults for both sexes.

22.10 Endoscopy in old age

- **Tolerance**: endoscopic procedures are generally well tolerated, even in very old people.
- **Side-effects from sedation**: older people are more sensitive, and respiratory depression, hypotension and prolonged recovery times are more common.
- **Bowel preparation for colonoscopy**: can be difficult in frail, immobile people. Sodium phosphate-based preparations can cause dehydration or hypotension and should be avoided in those with underlying cardiac or renal failure. Minimal preparation CT colonograms provide an excellent alternative in these individuals.
- **Antiperistaltic agents**: hyoscine should be avoided in those with glaucoma and can also cause tachyarrhythmias. Glucagon is preferred if an antiperistaltic agent is needed.

EBM **18.56 Angioplasty and intracoronary stents in angina**

'In comparison with simple balloon angioplasty, intracoronary stents afford superior acute and long-term clinical and angiographic results, with lower rates of re-stenosis (e.g. 17% vs 40%) and recurrent angina (13% vs 30%). Re-stenosis rates are reduced even further (< 10%) with drug-eluting stents.'

- Stettler C, et al. BMJ 2008; 337:a1331.

For further information: http://guidance.nice.org.uk/TA152

26.60 Multiple sclerosis in pregnancy

- **Counselling**: provision of pre-conception counselling is best practice.
- **Relapse risk**: endocrine effects on the immune system ensure that relapse risk drops during pregnancy.
- **Disease-modifying drugs**: risk of teratogenicity means that all disease-modifying drugs should ideally be stopped 6–8 wks before conception and recommenced after breastfeeding has stopped.
- **Post-partum relapse rate**: rebound of immune system activity means that the highest risk of relapse is in the first year after delivery.

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3. New '**In Adolescence' boxes** highlight the fact that many chronic disorders that begin in childhood go on to become the responsibility of physicians practising adult medicine. These boxes acknowledge the overlap 'transitional' phase and the key points for adult physicians when looking after young people.

19.40 Cystic fibrosis in adolescence

- **Issues for the patient**:
  - Move to adult CF centre – loss of trusted paediatric team
  - Feelings of being different from peers due to chronic illness
  - Demanding treatments that conflict with social and school life
  - Pressure to take responsibility for self-care
  - Relationship/fertility concerns
- **Issues for the patient's parents**:
  - Loss of control over patient's treatment – feeling excluded
  - Loss of trusted paediatric team
  - Need to develop trust in adult team
  - Feelings of helplessness when adolescent rebels or will not take treatment
- **Issues for the CF team**:
  - Reluctance or refusal by patient to engage with transition
  - Management of deterioration due to non-adherence
  - Motivation of adolescents to self-care
  - Provision of adolescent-friendly health-care environment

18.124 Congenital heart disease in adolescence

- **Patients**: a heterogeneous population with residual disease and sequelae that vary according to the underlying lesion and in severity; each patient must be assessed individually.
- **Management plan**: should be agreed with the patient and include a 'cardiac destination'.
- **Risks of surgery**: non-cardiac surgery, e.g. for associated congenital abnormalities, carries increased risks and needs to be planned, with careful pre-operative assessment. Risks include thrombosis, embolism from synthetic shunts or patches, and volume overload from fluid shifts. Operative approaches should address cosmetic concerns, e.g. abdominal generator implantation may be less unsightly.
- **Exercise**: patients with mild or repaired defects can undertake moderately vigorous exercise but those with complex defects, cyanosis, ventricular dysfunction or arrhythmias require specialist evaluation and individualised advice regarding exercise.
- **Genetics**: 10–15% have a genetic basis and this should be assessed to understand the impact it may have for the patient's own future children. A family history, genetic evaluation of syndromic versus non-syndromic disorders and, sometimes, cytogenetics are required.
- **Education and employment**: may be adversely affected and occupational activity levels need to be assessed.
- **End of life**: some adolescents with complex disorders may misperceive and think they have been cured; transition to adult services may be the first time they receive information about mortality. Expectations on life expectancy need to be managed and adolescents are often willing to engage with this and play a role in decision-making.

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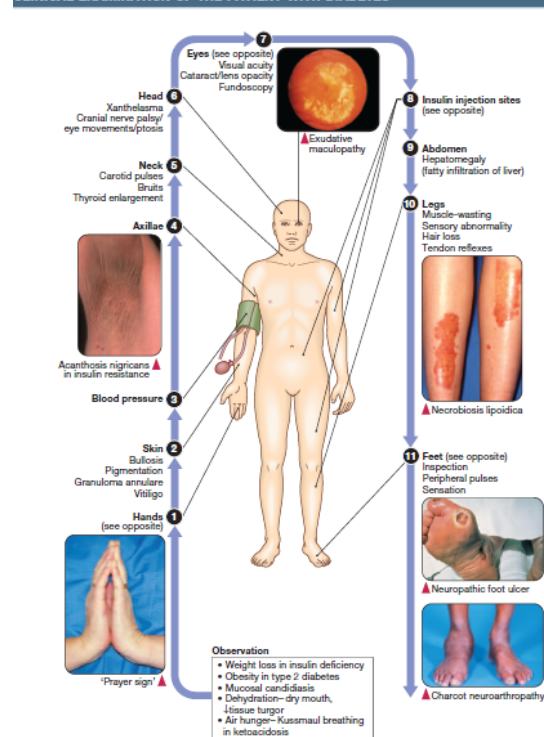
4. The very popular **Clinical Examination overviews** at the start of each of the systems-based chapters are retained, and have been refreshed with new images for the manikins on the left page and new examples of examination methods and interpretation on the right page.

CLINICAL EXAMINATION OF THE PATIENT WITH DIABETES

Diabetes can affect every system in the body. In routine clinical practice, examination of the patient with diabetes is focused on 1 hands, 3 blood pressure, 4 and 5 axillae and neck, 7 eyes, 8 insulin injection sites and 11 feet.

7 Examination of the eyes

Visual acuity

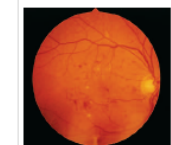
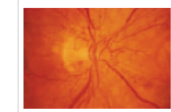
- Distance vision using Snellen chart at 6 metres
- Near vision using standard reading chart

Visual acuity can alter reversibly with acute hyperglycaemia due to osmotic changes affecting the lens. Most patients with retinopathy do not have altered visual acuity, except after a vitreous haemorrhage or in some cases of maculopathy.

Lens opacification

- Look for the red reflex using the ophthalmoscope held 30 cm from the eye

Fundal examination

- Either use a three-field retinal camera or dilate pupils with a mydriatic (e.g. tropicamide) and examine with ophthalmoscope in a darkened room
- Note features of diabetic retinopathy (p. 826), including photocoagulation scars from previous laser treatment

Background retinopathy.

Proliferative retinopathy.

1 Examination of the hands

Several abnormalities are more common in diabetes:

- Limited joint mobility ('cheiroarthropathy') causes painless stiffness. The inability to extend (to 180°) the metacarpophalangeal or interphalangeal joints of at least one finger bilaterally can be demonstrated in the 'prayer sign'
- Dupuytren's contracture (p. 1070) causes nodules or thickening of the skin and knuckle pads
- Carpal tunnel syndrome (p. 1228) presents with wrist pain radiating into the hand
- Trigger finger (flexor tenosynovitis)
- Muscle-wasting/sensory changes may be present in peripheral sensorimotor neuropathy, although this is more common in the lower limbs

8 Insulin injection sites

Main areas used

- Anterior abdominal wall
- Upper thighs/buttocks
- Upper outer arms

Inspection

- Bruising
- Subcutaneous fat deposition (lipohypertrophy)
- Subcutaneous fat loss (lipoatrophy; associated with injection of unpurified animal insulins – now rare)
- Erythema, infection (rare)

Lipohypertrophy.

11 Examination of the feet

Inspection

- Look for evidence of callus formation on weight-bearing areas, clawing of the toes (in neuropathy), loss of the plantar arch, discoloration of the skin (ischaemia), localised infection and ulcers
- Deformity may be present, especially in Charcot neuroarthropathy
- Fungal infection may affect skin between toes, and nails

Circulation

- Peripheral pulses, skin temperature and capillary refill may be abnormal

Sensation

- Abnormal in stocking distribution in typical peripheral sensorimotor neuropathy
- Testing light touch with monofilaments is sufficient for risk assessment; test other sensation modalities (vibration, pain, proprioception) only when neuropathy is being evaluated

Monofilaments. The monofilament is applied gently until slightly deformed at 5 points on each foot. Callus should be avoided as sensation is reduced. If the patient feels fewer than 8 out of 10 touches, the risk of foot ulceration is increased 5–10-fold.

Reflexes

- Loss of ankle reflexes in typical sensorimotor neuropathy
- Test plantar and ankle reflexes

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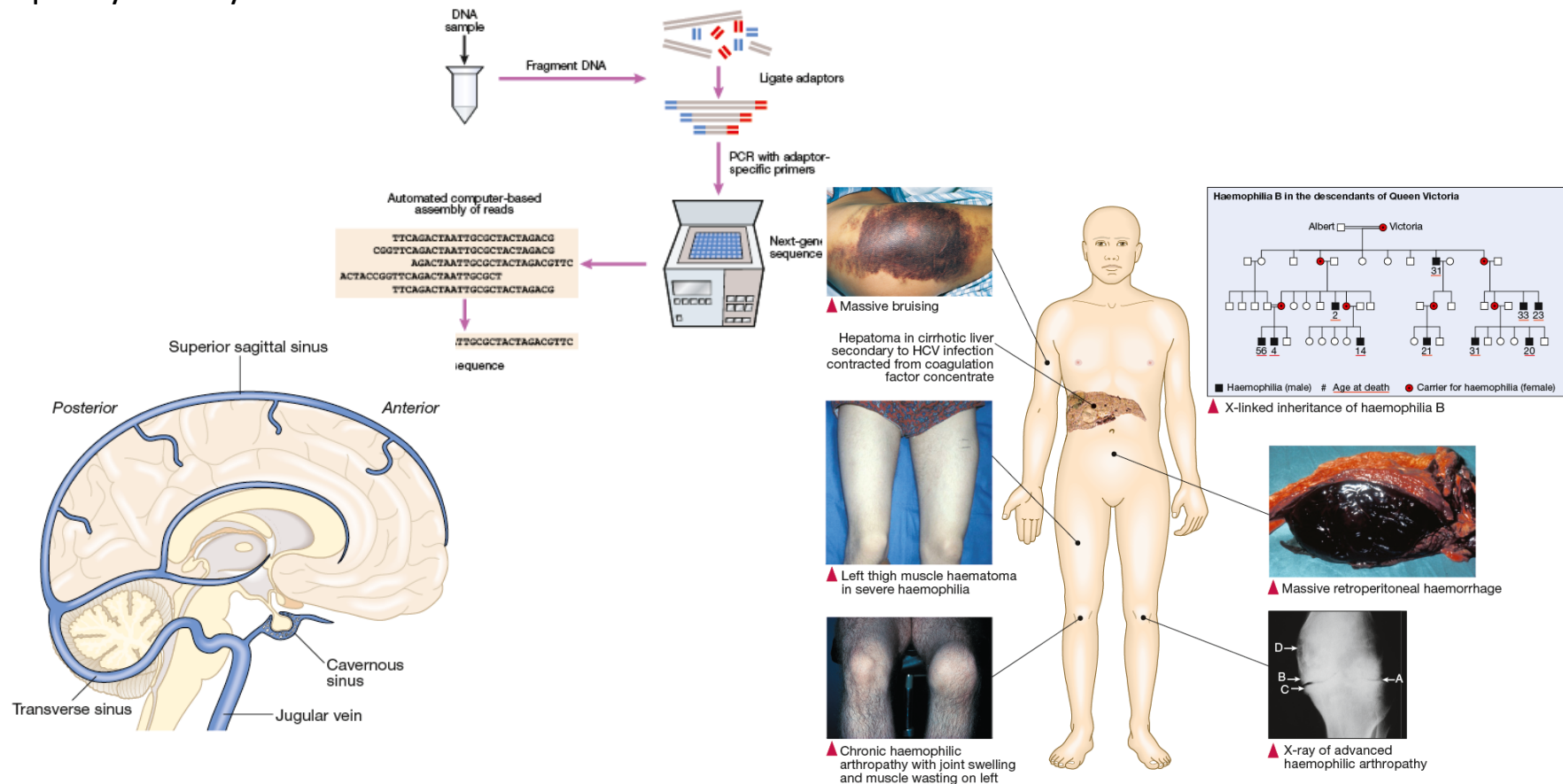
5. Robert Britton, whose **artwork** has underpinned the clarity of illustrations in Davidson's over many editions, has designed all of the new and revised figures, ensuring their consistency of quality and style.

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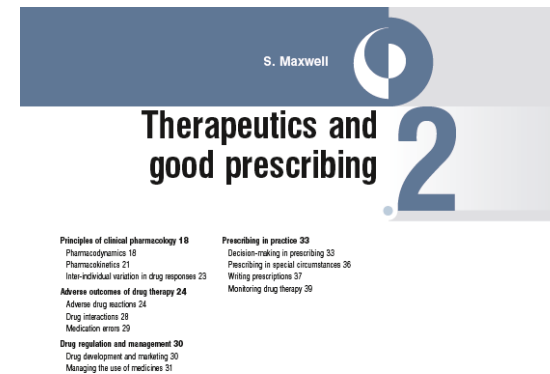
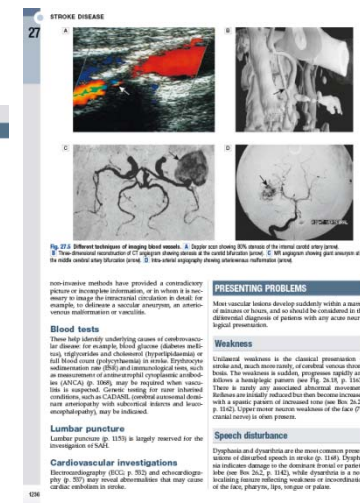
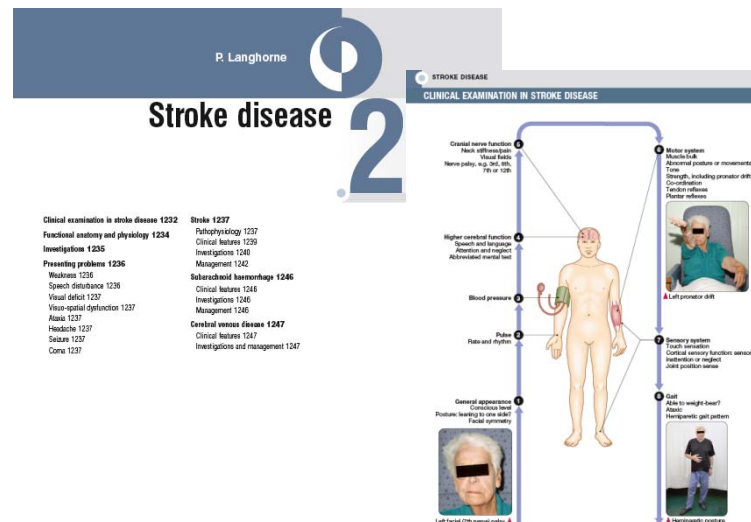
6. The regular introduction of **new authors and editors** maintains the freshness of each new edition. Dr Ian Penman has joined the editorial team and 18 new authors have helped to bring the content right up to date.

7. An **expanded International Advisory Board** now comprises 38 members from 16 different countries. Their systematic review of the 21st Edition produced important suggestions which were incorporated in chapter planning for the 22nd Edition.

Countries represented on the International Advisory Board:

- Australia
- Bangladesh
- Egypt
- Hong Kong
- India
- Japan
- Jordan
- Libya
- Malaysia
- New Zealand
- Pakistan
- Poland
- Saudi Arabia
- South Africa
- Sri Lanka
- Sweden

22 key points about the 22nd Edition

8. A new chapter on Therapeutics and Good Prescribing by Simon Maxwell provides a stronger emphasis on the underlying principles of Clinical Pharmacology and a more detailed description of the practicalities of drug prescribing. This recognises the central role of drug prescriptions in the practice of medicine, addresses recently documented deficiencies in prescribing skills of medical students and recent graduates, and helps readers to negotiate the increasingly complex polypharmacy that occurs in the ageing population.

9. A new chapter on Stroke Medicine by Peter Langhorne recognises the emergence of this discipline as a specific medical sub-specialty, and highlights the strong evidence base for contemporary therapy of stroke.

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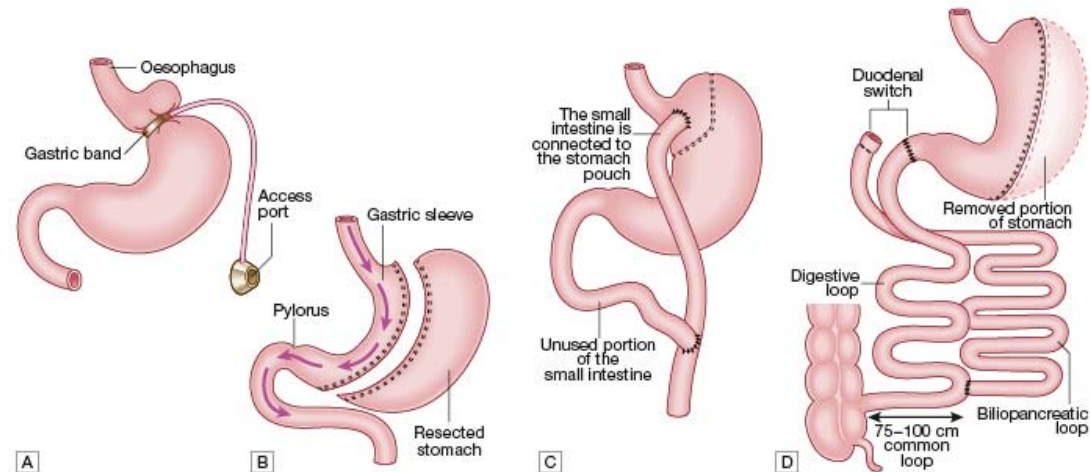
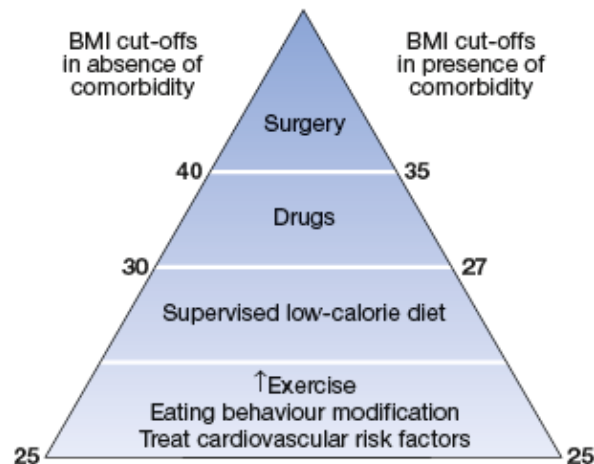
10. A new section on Obesity by John Wilding in the Environmental and Nutritional Factors in Disease chapter provides a practical guide to management of this highly prevalent problem, and new figures describe the increasing role of bariatric surgical procedures.

5.19 Some reasons for the increasing prevalence of obesity – the 'obesogenic' environment

Increasing energy intake	
• ↑ Portion sizes • ↑ Snacking and loss of regular meals	• ↑ Energy-dense food (mainly fat) • ↑ Affluence
Decreasing energy expenditure	
• ↑ Car ownership • ↓ Walking to school/work • ↑ Automation; ↓ manual labour	• ↓ Sports in schools • ↑ Time spent on computer games and watching TV • ↑ Central heating

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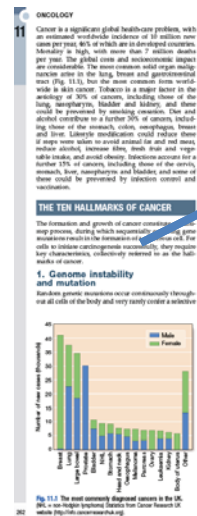
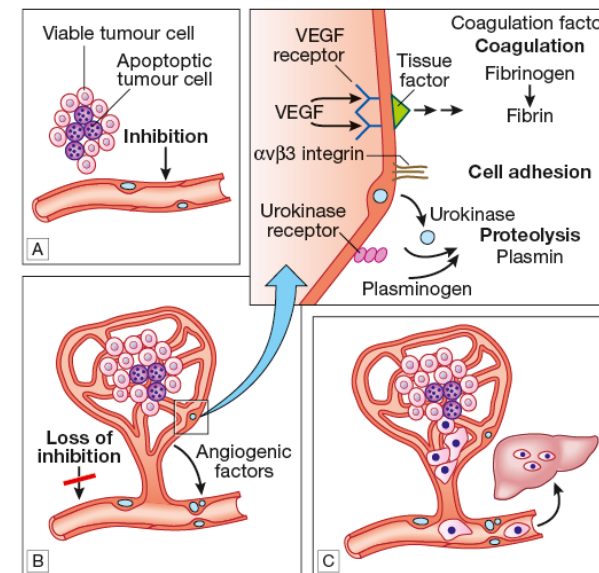
11. A new paradigm in cancer biology, “the ten hallmarks of cancer” is introduced in the Oncology chapter and eloquently describes the key mechanisms involved in cancer development and progression.

THE TEN HALLMARKS OF CANCER

The formation and growth of cancer constitute a multi-step process, during which sequentially occurring gene mutations result in the formation of a cancerous cell. For cells to initiate carcinogenesis successfully, they require key characteristics, collectively referred to as the hallmarks of cancer.

12. Management of elderly patients remains a ‘horizontal theme’ throughout the book, captured in the In Old Age boxes, but the introductory chapter on Ageing and Disease has been revised by new author Miles Witham, detailing the latest methods for assessing frailty, disability and rehabilitation needs.

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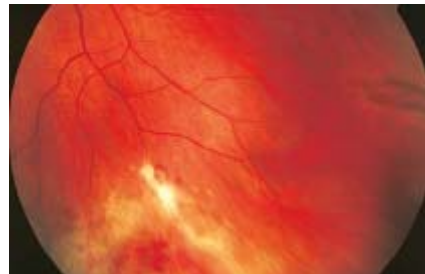
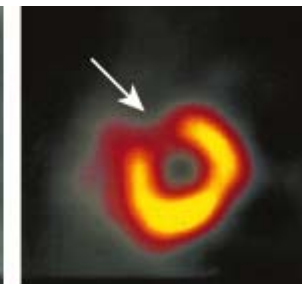
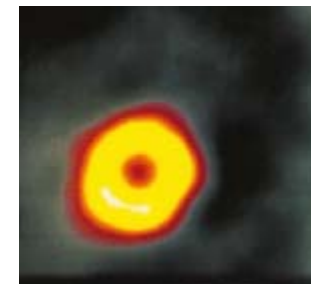
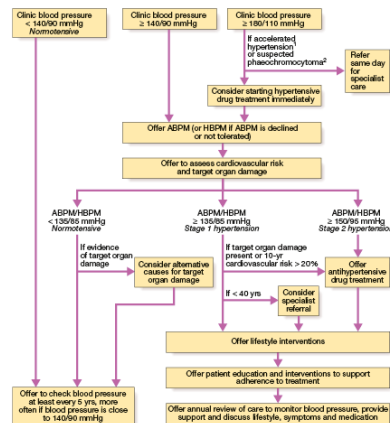
13. The **HIV/AIDS chapter** has been extensively revised by Gary Maartens, whose extensive experience of the condition in South Africa is reflected in a highly accessible and practical chapter.

14. New algorithms for adult life support, the management of acute coronary syndrome and hypertension, and the latest in cardiac CT and MR imaging, ensure the **Cardiology** chapter reflects state-of-the-art knowledge for all doctors.

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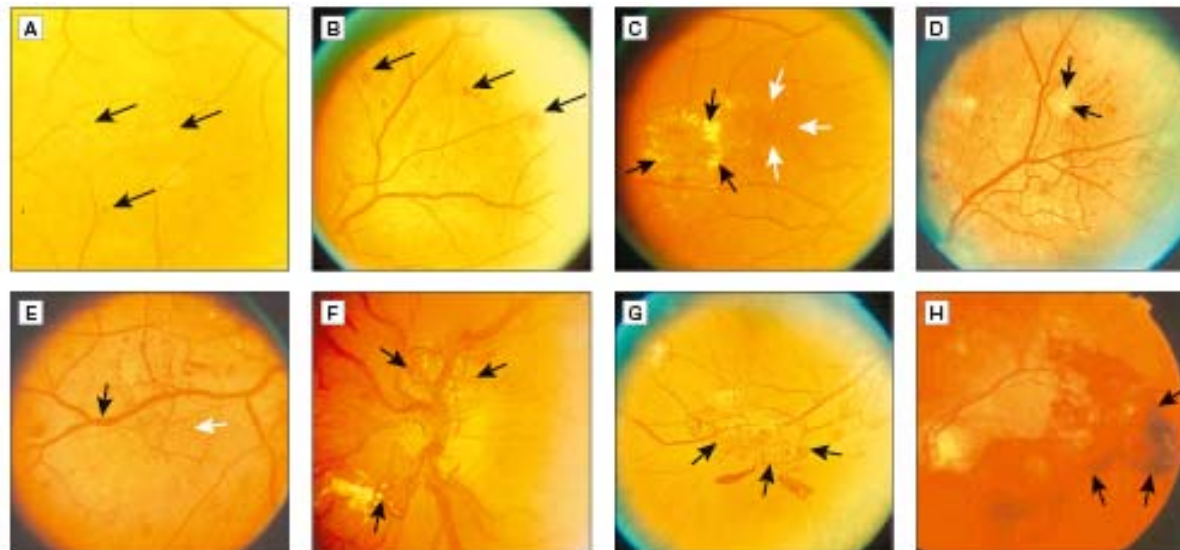
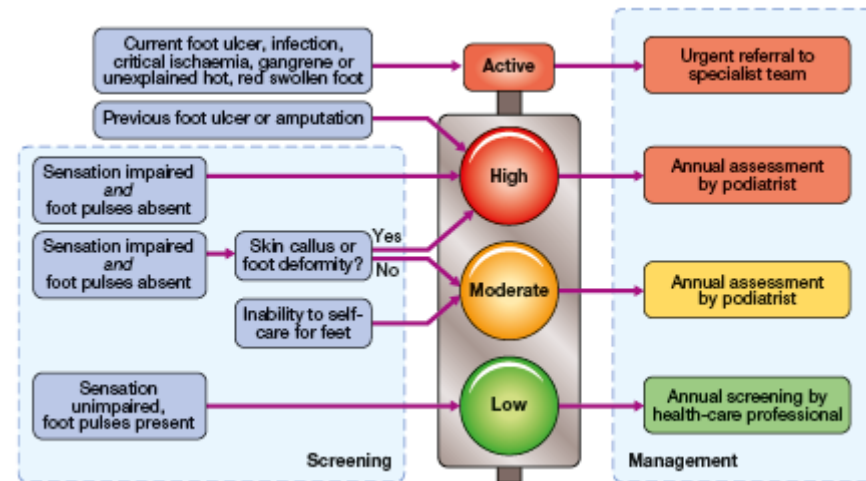
15. New authors of the **Diabetes** chapter, Rory McCrimmon and Ewan Pearson, have brought many practical guidelines to life in new illustrations and algorithms, conveying how all doctors should respond to this increasingly prevalent and resource-consuming disease.

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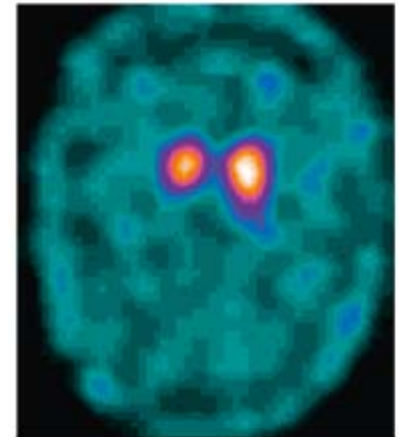
16. New authors David Jones and Quentin Anstee have extensively updated the chapter on **Liver Disease** to reflect the rapidly evolving fields of viral hepatitis, fatty liver and transplantation. A new approach to the assessment of patients is presented, highlighting the importance of careful clinical evaluation in determining acute from chronic liver disease.

17. The **Neurology** chapter has been thoroughly updated by new authors John Paul Leach and Richard Davenport, including new practical guidance on the challenges of the clinical approach and localisation of lesions in neurology.

18. The chapter on **Skin Disease** has been extensively restructured and updated by new authors, Sally Ibbotson and Robert Dawe. New sections on photosensitive and photo-aggravated conditions and the approach to common skin problems are matched by over 25 new high quality photographs.

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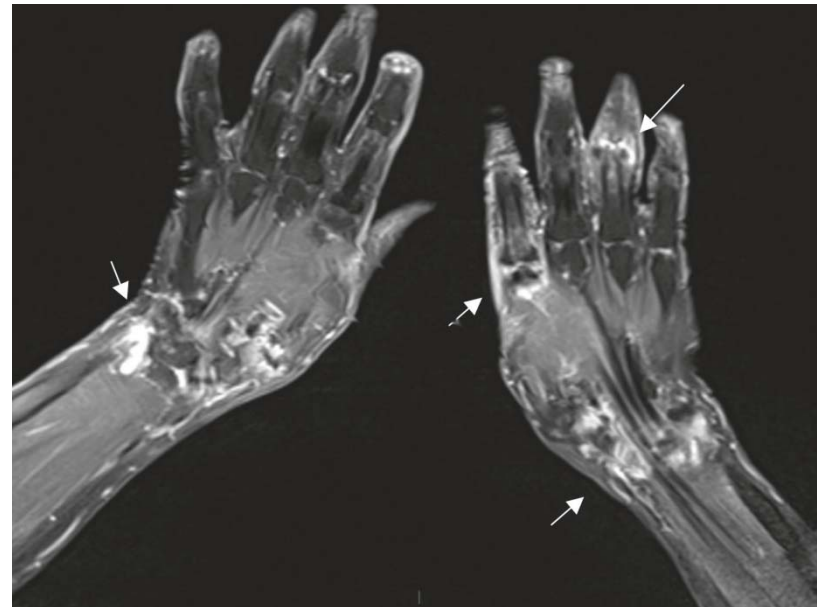
19. The chapter on **Kidney and Urinary Tract Disease** has been completely restructured to include a new examination section, an extensively revised section on presenting problems, and updated sections on diseases of the collecting system, prostate disease and tumours of the kidney and urinary tract.

20. The **Rheumatology and Bone Disease** chapter has been fully revised with new author Iain McInnes to include an updated section on imaging which emphasises the increasing importance of musculoskeletal ultrasound and MRI scanning in clinical practice, information on new diagnostic criteria for rheumatoid arthritis and seronegative spondyloarthropathies and an extensively updated section on drug treatment which puts the role of different drugs in context, and includes information on the latest biological therapies that are available.

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21. **Biological therapies** are introduced in the Therapeutics chapter and their use is explained in the Immunology chapter and where relevant throughout the book. The emergence and rapid expansion of this group of therapies for inflammatory diseases and cancer represents one the most significant developments in medicine in the last decade.

22. The revolution in medical genetics and the potential of ground-breaking cell-based therapies is reflected in an updated **Molecular and Genetic Mechanisms of Disease** chapter.

PRINCIPLES OF CLINICAL PHARMACOLOGY

Prescribers need to understand what the drug does to the body (pharmacodynamics) and what the body does to the drug (pharmacokinetics) (Fig. 2.1). Although this chapter is focused on the most common drugs, which are synthetic small molecules, the same principles apply to the increasingly numerous 'biological' therapies (sometimes abbreviated to 'biologics') now in use, which include peptides, proteins, enzymes and monoclonal antibodies (p. 74).

RESEARCH FRONTIERS IN MOLECULAR MEDICINE

Gene therapy

Replacing or repairing mutated genes (gene therapy) is very difficult in humans. Retroviral-mediated ex vivo replacement of the defective gene in bone marrow cells for the treatment of severe combined immune deficiency syndrome (p. 80) has been partially successful. There have been two major problems with the clinical trials of virally delivered gene therapy conducted to date:

- The random integration of the retroviral DNA (which contains the replacement gene) into the genome has caused leukaemia in some treated children via activation of proto-oncogenes.
- A severe immune response to the viral vector may be induced. It has not yet been possible to use non-viral means to introduce sufficient numbers of copies of replacement genes to produce significant biological effects.

Other therapies for genetic disease include PTC124, a compound that can 'force' cells to read through a mutation that results in a premature termination codon in an ORF with the aim of producing a near-normal protein product. This therapeutic approach could be applied to any genetic disease caused by nonsense mutations.

Cytokines

Cytokines are small soluble proteins that act as multi-purpose chemical messengers. Examples are listed in Box 4.2. They are produced by cells involved in immune responses and by stromal tissue. More than 100 cytokines have been described, with overlapping, complex roles in intercellular communication. Their clinical importance is demonstrated by the efficacy of 'biological' therapies (often abbreviated to 'biologics') that target specific cytokines (pp. 1102 and 18).